

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) ~~[[A]]~~ An osteoconductive and osteoinductive multilayer composite material comprising:

A) I) an inner matrix being a composite material and comprising:

(i) hyaluronic acid and/or hyaluronic acid derivatives, and

(ii) a matrix of demineralised bone and/or biocompatible and biodegradable ceramics and/or bone of autologous or allogenic or animal origin, and said matrix being sandwiched between

~~[[B)]]~~ II) one or more external at least two layers comprising a hyaluronic acid derivative

superimposed on said inner matrix, said hyaluronic acid derivative being in the form selected

from the group consisting of non-woven material, woven material, compact membrane or film, and perforated membrane or film.

2. (Withdrawn) The multilayer composite material according to claim 1, wherein the hyaluronic acid in (i) is salified with organic or inorganic bases.

3. (Currently Amended) The multilayer composite material, according to ~~any one of~~ claims claim 1 and 2, wherein said hyaluronic acid derivative in said inner matrix is selected from the group consisting of:

A) esters of hyaluronic acid,

B) inner esters of hyaluronic acid,

C) amides of hyaluronic acid,

D) O-sulphated derivatives of hyaluronic acid,

- E) deacetylated derivatives of hyaluronic acid, and
- F) percarboxylated derivatives of hyaluronic acid.

4. (Previously Presented) The multilayer composite material according to claim 3, wherein said hyaluronic acid ester is the benzyl ester.

5. (Previously Presented) The multilayer composite material according to claim 4, wherein the benzyl ester has a degree of esterification of from 50 to 100%.

6. (Previously Presented) The multilayer composite material according to claim 5, wherein the benzyl ester has a degree of esterification of from 75 to 100%.

7. (Withdrawn) The multilayer composite material as claimed in claim 3, wherein the hyaluronic acid inner esters have an esterification degree lower than 20%.

8. (Withdrawn) The multilayer composite material as claimed in claim 7, wherein the hyaluronic acid inner esters have an esterification degree comprised between 0.05 and 5%.

9. (Withdrawn) The multilayer composite material as claimed in claim 3, wherein the amidation degree of hyaluronic acid amides (C) is lower than or equal to 15%.

10. (Withdrawn) The multilayer composite material as claimed in claim 9, wherein the amidation degree is comprised between 0, 1, and 15%.

11. (Withdrawn) The multilayer composite material as claimed in claim 3, wherein the deacetylated hyaluronic acid has a percentage of deacetylation lower than or equal to 30%.
12. (Withdrawn) The multilayer composite material as claimed in claim 3, wherein the percarboxylated hyaluronic acid (F) has a percarboxylation degree of between 0.1 and 100%.
13. (Withdrawn) The multilayer composite material as claimed in claim 12, wherein said percarboxylation degree is comprised between 25 and 75%.
14. (Previously Presented) The multilayer composite material according to claim 1, wherein the biocompatible and biodegradable ceramics is selected from the group consisting of hydroxyapatite and/or anhydrous tribasic calcium phosphate and/or calcium sulphate.
15. (Withdrawn) The multilayer composite material according to claim 1, wherein the bone matrix is partially or completely demineralised.
16. (Previously Presented) The multilayer composite material according to claim 1, wherein the hyaluronic acid derivative has a molecular weight of between 200 and 750 KD.
17. (Currently Amended) The multilayer composite material according to claim 1, wherein the hyaluronic acid derivative in the inner matrix (I) is in a form selected from the group consisting of ~~a non-woven tissue, a sponge, a paste, and/or a gel granules, and powders.~~

18. (Canceled).

19. (Currently Amended) The multilayer composite material according to claim 1, comprising 2 external layers (II) ~~(B)~~.

20. (Currently Amended) The multilayer composite material according to claim 1, comprising 3 external layers (II) ~~(B)~~.

21. (Currently Amended) The multilayer composite material, according to claim 1, wherein said hyaluronic acid derivative contained in said at least two ~~one or more external~~ layers (II) is selected from the group consisting of:

- A) esters of hyaluronic acid,
- B) inner esters of hyaluronic acid,
- C) amides of hyaluronic acid,
- D) O-sulphated derivatives of hyaluronic acid,
- E) deacetylated derivatives of hyaluronic acid, and
- F) percarboxylated derivatives of hyaluronic acid.

22. (Previously Presented) The multilayer composite material according to claim 21, wherein said hyaluronic acid ester is the benzyl ester.

23. (Previously Presented) The multilayer composite material according to claim 22, wherein the benzyl ester has a degree of esterification of from 50 to 100%.

24. (Previously Presented) The multilayer composite material according to claim 23, wherein the benzyl ester has a degree of esterification of from 75 to 100%.

25. (Withdrawn) The multilayer composite material according to claim 21, wherein the hyaluronic acid inner esters have an esterification degree lower than 20%.

26. (Withdrawn) The multilayer composite material according to claim 25, wherein the hyaluronic acid inner esters have an esterification degree comprised between 0.05 and 5%.

27. (Withdrawn) The multilayer composite material according to claim 21, wherein the amidation degree of hyaluronic acid amides (C) is lower than or equal to 15%.

28. (Withdrawn) The multilayer composite material according to claim 27, wherein the amidation degree is comprised between 0,1 and 15%.

29. (Withdrawn) The multilayer composite material according to claim 21, wherein the deacetylated hyaluronic acid has a percentage of deacetylation lower than or equal to 30%.

30. (Withdrawn) The multilayer composite material according to claim 21, wherein the percarboxylated hyaluronic acid (F) has a percarboxylation degree of between 0.1 and 100%.

31. (Withdrawn) The multilayer composite material according to claim 30, wherein said percarboxylation is comprised between 25 and 75%.

32. (Cancelled).

33. (Currently Amended) The multilayer composite material according to claim 1, wherein the inner matrix is in the form of a sponge consisting of the benzyl ester of hyaluronic acid with a percentage of esterification ranging between 70 and 100%, containing inside said sponge:

~~⊖~~ bone granules or powders that are autologous and/or allogenic and/or of animal origin; or granules or other three-dimensional structures constituted by biodegradable ceramics; or partially or completely demineralised bone matrix.

34. (Previously Presented) The multilayer composite material according to claim 1, subsequently coated throughout with hyaluronic acid and/or the derivatives thereof; in the form of a thin film and/or sponge, to favour the entry, distribution, and adhesion of the cells that will migrate once they have been loaded therein.

35. (Withdrawn) The multilayer composite materials according to claim 1, wherein the inner matrix is in the form of sponges formed by the inner esters of HA containing inside them: bone granules and/or powders of autologous and/or allogenic type and/or of animal origin; biodegradable ceramics; or partially or completely demineralised bone matrix.

36. (Withdrawn) The multilayer composite materials according to claim 1, wherein the inner matrix is in the form granules, spheres, powders, and/or three-dimensional structures of various shapes and sizes consisting of biodegradable ceramics that are coated/incorporated in a

layer of HA subsequently cross-linked to form its inner ester (ACP®), which thus covers all the ceramic structures.

37. (Currently Amended) The multilayer composite materials according to claim 1, wherein the inner matrix is in the form of pastes and/or gels consisting of hyaluronic acid and hyaluronic acid derivatives enclosing bone powders and/or granules that are autologous and/or allogenic and/or of animal origin; or granules or other three-dimensional structures constituted by biodegradable ceramics or, lastly, pastes and/or gels containing demineralised bone matrix.

38. (Withdrawn) The multilayer composite materials according to claim 1, wherein the inner matrix is in the form of fibres comprising the benzyl ester of hyaluronic acid (HA) with a percentage of esterification ranging between 50 and 100%, possibly associated with other natural polymers selected from collagen and cellulose and the derivatives thereof, or synthetic polymers selected from poly-lactic, polyglycolic and poly-caprolactone acid, in association with demineralized bone matrix and hyaluronic acid.

39. (Withdrawn) The multilayer composite materials according to claim 38, wherein the matrix can be wetted with a solution of hyaluronic acid ester, to render it more compact with the layers between which it is sandwiched.

40. (Withdrawn) The multilayer composite materials according to claim 38, wherein said matrix consists of fibres of hyaluronic acid benzylester having an esterification degree of 75% in amounts ranging from 10 to 50% and demineralised bone matrix in amounts ranging from 50 to

90% and hyaluronic acid having an average molecular weight ranging from 200 to 750 KD in amounts ranging from 0.1 and 40%.

41. (Withdrawn) The multilayer composite material according to claim 40, wherein said matrix consists of fibres of hyaluronic acid benzylester having an esterification degree of 75% in amounts ranging from 14 to 24%, demineralised bone matrix in amounts varying between 60 and 80%, hyaluronic acid having an average molecular weight ranging from 500 to 700 KD in amounts comprised between between 5 and 10%.

42. (Currently Amended) The multilayer composite material according to claim 1, wherein said inner matrix is immersed to make the final matrix more compact and fixable to the layers (II).

43. (Withdrawn) The multilayer composite according to claim 42, wherein said polymer is selected from: hyaluronic acid benzyl ester with a percentage of esterification of between 55 and 100%; fibrin glue; photocross-linkable polymers; collagen and derivatives thereof.

44. (Currently Amended) The multilayer composite material according to claim 1, wherein said at least two ~~one or more~~ layers (II) comprise a hyaluronic acid ester.

45. (Previously Presented) The multilayer composite material according to claim 44, wherein said hyaluronic acid is the benzylester with a percentage of esterification ranging between 50 and 100%.

46. (Previously Presented) The multilayer composite material according to claim 45, wherein said percentage degree is comprised between 75 and 100%.

47. (Currently Amended) The multilayer composite material according to claim 44, wherein the layers (II) are in the form of: a non-woven material, containing fibres of the hyaluronic acid ester possibly associated with natural polymers selected from collagen ~~collagene~~ and cellulose and the derivatives thereof, or synthetic polymers selected from poly-lactic acid, poly-glycolic acid, and poly-caprolactone acid.

48. (Currently Amended) The multilayer composite material according to claim 44, wherein the layers (II) are in the form of a woven material containing fibres of the hyaluronic acid ester, possibly subsequently immersed in a solution of hyaluronic acid.

49. (Currently Amended) The multilayer composite material according to claim 1, wherein the layers are in the form of compact perforated porous or microporous membranes or ~~[[and]]~~ films.

50. (Previously Presented) The multilayer composite materials according to claim 1, further containing pharmacologically and/or biologically active ingredients.

51. (Previously Presented) The multilayer composite materials according to claim 50, wherein the pharmacologically active ingredients are selected from the group consisting of

antibiotics, antineoplastics, anti-inflammatories, cytokines, vitamins and cytotoxic, cytostatic and antiviral agents.

52. (Currently Amended) The multilayer composite materials according to claim 50, wherein biologically active ingredients contain trophic, osteoinductive, and/or angiogenic factors.

53. (Currently Amended) The multilayer composite material according to claim 52, wherein the trophic, osteoinductive, and/or ~~[[and]]~~ angiogenic factors are selected from ~~contain~~ bone morphogenetic protein, transforming growth factor, platelet derived growth factor, fibroblast growth factor, epidermal growth factor, insulin-like growth factor, and vascular endothelial growth factor.

54-60. (Canceled).

61. (Previously Presented) A bone substitute or graft consisting of the multilayer composite material according to claim 1.

62. (Canceled).

63. (Previously Presented) The bone substitute or graft according to claim 61 in the form of a sandwich or bag.

64-82. (Canceled).

83. (New) The multilayer composite material according to claim 1, wherein the hyaluronic acid derivative is in the form of fibres.

84. (New) The multilayer composite material according to claim 1, wherein the inner matrix (I) is in the form of a paste.

85. (New) The multilayer composite material according to claim 1, wherein the at least two layers (II) comprise the hyaluronic acid derivative in the form of woven material.

86. (New) The multilayer composite material according to claim 1, wherein the hyaluronic acid derivative ranges between 10 and 50% of the inner matrix (I), the demineralised bone and/or biocompatible and biodegradable ceramics and/or bone of autologous or allogenic or animal origin ranges between 50 and 90% of the inner matrix (I), and the hyaluronic acid ranges between 0.1 and 40% of the inner matrix (I).

87. (New) The multilayer composite material according to claim 86, wherein the hyaluronic acid derivative ranges between 14 and 24% of the inner matrix (I), the demineralized bone and/or biocompatible and biodegradable ceramics and/or bone of autologous or allogenic or animal origin ranges between 60 and 80% of the inner matrix (I), and the hyaluronic acid ranges between 5 and 10% of the inner matrix (I).

88. (New) The multilayer composite material according to claim 1, wherein the inner matrix (I) is in the form of a paste comprising benzyl ester of hyaluronic acid in the form of fibres, hyaluronic acid and demineralised bone, and wherein the at least two layers (II) comprise the hyaluronic acid derivative in the form of woven material.